

REMARKS

Applicants have amended the specification and claims to provide corrected SEQ ID numbers for the nucleotides referred to therein. As such, these amendments do not constitute new matter and their entry is respectfully submitted.

In view of the foregoing amendment it is respectfully submitted that all claims are in condition for allowance. Early and favorable action is requested.

If any additional fee is required, charge Deposit Account No. 50-0850.

Respectfully submitted,



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VERSION TO SHOW MARKED CHANGES IN THE SPECIFICATION AND CLAIMS

Page 8, paragraph 6:

Fig. 20 shows SEQ ID NOS: 3 and 4, the nucleotide and amino-acid sequence, respectively, of G β 3s-2.

Page 8, paragraph 9:

The polymorphism C1429T is referenced to the cDNA sequence as was described by Levine et al. Here replacement of the C by a T takes place on position 1429 of the cDNA: 1381 [qq]ggcctgggtg gtataggcg ttggccctg tgactatggc tctggcac(c/t)a cttaggtcct (SEQ ID NO: 5)

Page 8, paragraph 11:

Referenced to the genomic sequence of the GBN3 locus as was described by Ansari-Lari et al (Ansari-Lari, M.A., Muzny, D.M., Lu, J., Lu, F., Lilley, C.E., Spanos, S., Malley, T. and Gibbs, R.A. A gene-rich cluster between the CD4 and triosephosphate isomerase genes at human chromosome 12p13. Genome Res. 6(4), 314-326 (1996)), this polymorphism is located as follows (C59308T):

59281 TTGGCCCTGT GACTATGGCT CTGGCAC(C/T)AC TAGGGTCCTG GCCCTCTTCT
TATTCA TGCT (SEQ ID NO: 6)

Page 36, paragraph 6:

To do this, the mRNA was extracted using standard methods from neutrophilic granulocytes of individuals who are homozygotic for the C825 in GNB3 (CC genotype) or who are heterozygotic for the C825T polymorphism (TC genotype) and are transcribed by means of the reverse transcriptase reaction in cDNA. The cDNA which codes for G β 3 was amplified by means of a polymerase chain reaction. Here the following primers were used:

Sense: 5' - gcc gtc aga ctt tca ctg gc - 3' (SEQ ID NO: 7)

Antisense: 5' - tgt tca ctg cct tcc act tcc - 3' (SEQ ID NO: 8)

IN THE CLAIMS:

2. A method for diagnosing an increased likelihood of developing a disease associated with G protein dysregulation comprising determining the presence of a genetic modification in a

gene obtained from a subject which encodes the Gbeta3 subunit of the human G protein, wherein said genetic modification is a substitution of cytosine by thymine at position 1429 of SEQ ID NO:1[2].

5. A method for diagnosing an increased likelihood of a woman developing a cardiovascular condition, comprising determining the presence of a genetic modification in a G protein beta3 subunit obtained from the woman, wherein said genetic modification is a cystosine to thymine substitution of position 1429 of SEQ ID NO:1[2].
6. The method of claim 5, wherein said genetic modification is at position 825 of SEQ ID NO: 1[2].
18. A method for evaluating responsiveness of an individual to an in vivo pharmaceutical comprising evaluating the individual for a genetic modification in a gene encoding a Gbeta3 subunit of a protein, wherein the genetic modification is a substitution of cytosine by thymine at position 825 and/or at position 1429 of SEQ ID NO:1[2].
19. A method for evaluating responsiveness of an individual to in vivo to hormones, transmitters, neurotransmitters or pharmaceuticals which activate those G protein heterotrimers which contain the G protein subunits Gbeta3 and Gbeta3s and/or which stimulate the G protein subunit Galphas comprising evaluating the individual for a genetic modification in a gene encoding a Gbeta3 subunit of a protein, wherein the genetic modification is a substitution of cytosine by thymine at position 825 and/or at position 1429 of SEQ ID NO:1[2].
25. A method for evaluating responsiveness of an individual to treatment with beta-adrenoceptor blockers comprising evaluating the individual for a genetic modification in a gene encoding a Gbeta3 subunit of a human G protein, wherein the genetic modification is a substitution of cytosine by thymine position 825 and/or position 1429 of SEQ ID NO:1[2].